AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application.

1. (Currently amended) A method of treatment or prevention of at least one degenerative disorder of muscle, bone, or glucose homeostasis associated with GDF-8, ~~comprising~~ comprising:

   (1) administering an effective amount of a pharmaceutical composition to a mammal, wherein the composition comprises an ActRIIB fusion polypeptide comprising (a) ~~a first~~ an amino acid sequence ~~derived from the ActRIIB extracellular domain~~ that is at least 80% identical to amino acids 23 to 138 of SEQ ID NO:3 and is capable of binding to GDF-8, and (b) ~~a second amino acid sequence derived from the~~ an Fc portion of an antibody; and

   (2) allowing the composition to inhibit GDF-8 activity.

2. (Original) The method of claim 1, wherein the mammal is human.

3. (Original) The method of claim 1, wherein the pharmaceutical composition is administered to a mammal in need of treatment or prevention of a disorder chosen from at least one of muscle disorder, neuromuscular disorder, and bone degenerative disorder.

4. (Original) The method of claim 1, wherein the pharmaceutical composition is administered to a mammal in need of treatment or prevention of a disorder chosen from at least one of muscular dystrophy, Duchenne's muscular dystrophy, muscle atrophy, organ atrophy, carpal tunnel syndrome congestive obstructive pulmonary disease, sarcopenia, cachexia, muscle wasting syndrome, and amyotrophic lateral sclerosis.

5. (Original) The method of claim 1, wherein the pharmaceutical composition is administered to a mammal in need of treatment or prevention of Duchenne's muscular dystrophy.

6. (Original) The method of claim 1, wherein the pharmaceutical composition is administered to a mammal in need of treatment or prevention of a disorder chosen from at least one of obesity and adipose tissue disorder.

7. (Original) The method of claim 1, wherein the pharmaceutical composition is administered to a mammal in need of treatment or prevention of a disorder chosen from at least one of syndrome X, impaired glucose tolerance, trauma-induced insulin resistance, and type 2 diabetes.

8. (Currently amended) The method of claim 1, wherein the pharmaceutical composition is administered to a mammal in need of treatment or prevention of at least one of type 2 ~~dibetes~~ diabetes and obesity.

9. (Original) The method of claim 1, wherein the pharmaceutical composition is administered to a mammal in need of treatment or prevention of a disorder chosen from at least one of osteoarthritis and osteoporosis.

10. (Original) The method of claim 1, wherein the pharmaceutical composition is administered to a mammal in need for repair of damaged muscle.

11. (Currently amended) The method of ~~claim 9~~ claim 10, wherein the damaged muscle is myocardiac muscle or diaphragm.

12. (Currently amended) The method of claim 1, wherein ~~said~~ the ActRIIB fusion polypeptide is administered at [[the]] an effective amount chosen from 1 [[μ/kg]] μg/kg to 20 mg/kg, 1 μg/kg to 10 mg/kg, 1 μg/kg to 1 mg/kg, 10 μg/kg to 1 mg/kg, 10 μg/kg to 100 μg/kg, 100 μg to 1 mg/kg, and 500 μg/kg to 1 mg/kg.

13. (Original) The method of claim 1, wherein the first amino acid sequence of said ActRIIB fusion polypeptide comprises amino acids 23 to 138 of SEQ ID NO:3.

14. (Original) The method of claim 1, wherein the first amino acid sequence of said ActRIIB fusion polypeptide comprises amino acids 19 to 144 of SEQ ID NO:1.

15. (Original) The method of claim 1, wherein the second amino acid sequence of said ActRIIB fusion polypeptide comprises a sequence chosen from (a) the Fc fragment of IgG, (b) the Fc fragment of IgG_1, (c) the Fc fragment of IgG_4, and (d) amino acids 148 to 378 of SEQ ID NO:3.

16. (Original) The method of claim 1, wherein the sequence of the ActRIIB fusion polypeptide is set out in SEQ ID NO:3.

17. (Original) The method of claim 1, wherein circulatory half-life of the ActRIIB fusion polypeptide exceeds 5 days.

18-22. (Cancelled)

23. (Currently amended) The method of claim 1, wherein the fusion protein is encoded by a nucleic acid that hybridizes to the [[~~sequence~~]] complement of SEQ ID NO:4 under stringent hybridization conditions.

24. (Cancelled)

25. (Currently amended) A method of inhibiting GDF-8 activity, ~~comprising~~ comprising:

(1) contacting GDF-8 with a composition, wherein the composition comprises an ActRIIB fusion polypeptide comprising (a) ~~a first~~ an amino acid sequence ~~derived from the ActRIIB extracellular domain~~ that is at least 80% identical to amino acids 23 to 138 of SEQ ID NO:3 and is capable of binding to GDF-8, and (b) ~~a second amino acid sequence derived from the~~ an Fc portion of an antibody; and

(2) allowing the composition to inhibit GDF-8 activity.

26. (Currently amended) A method of increasing muscle strength, said method ~~comprising~~ comprising:

(1) administering ~~a therapeutically~~ an effective amount of ~~the ACtRIIB~~ a pharmaceutical composition to a mammal, wherein the composition comprises an ActRIIB fusion polypeptide ~~to a mammal, thereby increasing muscle strength, wherein the ActRIIB fusion polypeptide~~ comprising (a) ~~a first~~ an amino acid sequence ~~derived from the ActRIIB extracellular domain~~ that is at least 80% identical to amino acids 23 to 138 of SEQ ID NO:3 and is capable of binding to GDF-8, and (b) ~~a second amino acid sequence derived from the~~ an Fc portion of an antibody; and

(2) allowing the composition to inhibit GDF-8 activity,

thereby increasing muscle strength.

27. (Currently amended) A method of increasing trabecular bone density, said method ~~comprising~~ comprising:

(1) [[~~a~~]] administering ~~a therapeutically~~ an effective amount of ~~the ActRIIB~~ a pharmaceutical composition to a mammal, wherein the composition comprises an ActRIIB fusion polypeptide ~~to a mammal, thereby increasing trabecular bone density, wherein the ActRIIB fusion polypeptide~~ comprising (a) ~~a first~~ an amino acid sequence ~~derived from the ActRIIB extracellular domain~~ that is at least 80% identical to amino acids 23 to 138 of SEQ ID NO:3 and is capable of binding to GDF-8, and (b) ~~a second amino acid sequence derived from the~~ an Fc portion of an antibody; and

(2) allowing the composition to inhibit GDF-8 activity,

thereby increasing trabecular bone density.

28. (Currently amended) A method of increasing glucose tolerance, said method ~~comprising~~ comprising:

(1) [[~~a~~]] administering ~~a therapeutically~~ an effective amount of ~~the ActRIIB~~ a pharmaceutical composition to a mammal, wherein the composition comprises an ActRIIB fusion polypeptide ~~of to a mammal, thereby increasing trabecular bone density, wherein the ActRIIB fusion polypeptide~~ comprising (a) ~~a first~~ an amino acid sequence ~~derived from the ActRIIB extracellular domain~~ that is at least 80% identical to amino acids 23 to 138 of SEQ ID NO:3 and is capable of binding to GDF-8, and (b) ~~a second amino acid sequence derived from the~~ an Fc portion of an antibody; and

(2) allowing the composition to inhibit GDF-8 activity,

thereby increasing glucose tolerance.

29. (New) The method of claim 1, wherein the amino acid sequence is at least 85% identical to amino acids 23 to 138 of SEQ ID NO:3.

30. (New) The method of claim 1, wherein the amino acid sequence is at least 90% identical to amino acids 23 to 138 of SEQ ID NO:3.

31. (New) The method of claim 1, wherein the amino acid sequence is at least 95% identical to amino acids 23 to 138 of SEQ ID NO:3.

32. (New) The method of claim 1, wherein the Fc portion is modified to reduce effector function.

33. (New) The method of claim 1, wherein the Fc portion is modified to reduce binding to an Fc receptor.

34. (New) The method of claim 1, wherein the Fc portion is modified to reduce complement activation.

35. (New) The method of claim 1, wherein the Fc portion is unmodified.